

### REMARKS

Pursuant to the requirements under 37 C.F.R. §§ 1.821-1.825, Applicant submits herewith a paper copy of a Sequence Listing. A computer readable copy of same Sequence Listing was submitted on May 15, 2001 in U.S. Serial No. 09/411,688, which is the parent of the instant application. The content of the paper and computer readable copies of the Sequence Listing are the same. Kindly amend the application by entry of the paper sequence listing after the claims. Applicant also requests that the computer readable copy of filed in parent application U.S. Serial No. 09/411,688 be transferred to the instant application, pursuant to 37 C.F.R. § 1.821(e). Applicant respectfully submits that no new matter will be introduced into the application as filed via entry of the Sequence Listing.

In addition, Applicant has amended the specification to include references to the sequences set forth in the sequence listing. Support for the amendments to the specification can be found throughout the application as filed. Applicant respectfully submits that no new matter has been added via this amendment to the application.

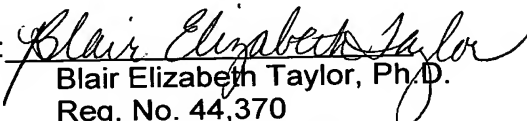
Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached Appendix is captioned **“Version with markings to show changes made”**.

Applicant respectfully submits that the present application is in a condition for allowance and a Notice to that effect is earnestly solicited.

Should any questions regarding the patentability of the claims arise, the Examiner is invited to telephone the undersigned to discuss the same.

Respectfully submitted,

PILLSBURY WINTHROP LLP

By:   
Blair Elizabeth Taylor, Ph.D.  
Reg. No. 44,370  
Tel: (703) 905-2198  
Fax: (703) 905-2500

1600 Tysons Boulevard  
McLean VA 22102  
Tel: (703) 905-2000  
Enclosures: Appendix, Sequence Listing

**APPENDIX**  
**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE SPECIFICATION:**

The specification is changed as follows:

The paragraph at page 4, line 24 *et seq.* has been amended to read:

In particular, the invention relates to the medical, pharmaceutical and cosmetic uses of trypsins derived from Atlantic cod or other animals. There are three isoenzymes of trypsin in Atlantic cod that have been purified and characterized. They have been termed Trypsin I, II and III (Ásgeirsson et al., Eur. J. Biochem. 180:85-94, 1989). The cod trypsins have the amino terminal sequence I-V-G-G-Y-Q/E-C-E/T-K/R-H-S-Q-A-H-QV-S-L-N-S (SEQ ID NO.:1) while mammalian trypsins such as bovine trypsin have the amino terminal sequence I-V-G-G-Y-T-C-G-A-N-T-V-P-Y-Q-V-S-L-N-S (SEQ ID NO.: 2). All three isoforms of cod trypsin have a similar molecular mass of about 24 kDa.

The paragraph at page 5, line 2 *et seq.* has been amended to read:

The invention also relates to the medical, pharmaceutical and cosmetic uses of chymotrypsins derived from Atlantic cod or other animals. There are two major isoenzymes of chymotrypsin in Atlantic cod that have been purified and characterized. They have been designated Chymotrypsin A and B (Ásgeirsson and Bjarnason, Comp. Biochem. Physiol. 99B:327-335-94, 1991). The cod chymotrypsins have the dual amino terminal sequences of one of its active forms

C-G-R/S-P-A-I-S/Q-P-V/Q-I/V-T-G-Y (A chain, SEQ ID NO.: 3) and I-V-N-G-E-E-A-V-P-H-S/T-W-S/P/Y-W-Q-V-S-LQ-D/Q (B chain, SEQ ID NO.: 4) whereas mammalian chymotrypsins such as bovine chymotrypsin A have the amino terminal sequences C-G-V-P-A-I-Q-P-V-L-S-G-L (A chain, SEQ ID No.: 5) and I-V-N-G-E-E-A-V-P-G-S-W-P-W-Q-V-S-L-Q-D (B chain, SEQ ID NO.: 6). Both isoforms of cod chymotrypsin have a similar molecular mass of about 26 kDa.

The paragraph at page 5, line 24 *et seq.* has been amended to read:

The preferred method of application of the purified enzymes or mixture of purified enzymes is in a preparation of hydrogel and water containing 0 to 85% (vol/vol) of a polyvalent alcohol (polyol) such as glycerol. A suitable concentration of trypsin activity is 0.1 to 10,000 enzyme units of activity for CBZ-Gly-Pro-Arg-pNA (carbobenzoxyl Gly-Pro-Arg-para nitroanilide) per 100 milliliters of the final hydrogel preparation and the appropriate concentration of chymotrypsin activity is 0.1 to 10,000 enzyme units of activity for Succinyl-Ala-Ala-Pro-Phe-pNA (SEQ ID NO.: 7) per 100 milliliters of the final hydrogel preparation.

The paragraph at page 12, line 21 *et seq.* has been amended to read:

The molecular mass of the cod trypsins is about 24 kDa, whereas their isoelectric points are 6.6, 6.2 and 5.5 for trypsin I, II and III respectively. The amino acid sequences of the three isozymes of cod trypsin can be expressed with the following sequence (SEQ ID NO.: 8) which contains point variability due to the multiple isoforms: